REMARKS

Status of the Claims

Claims 34-35, 37-40, 42-44, 46, 49-51, 54, 56-58, and 60-61 are pending in the present application, Claims 1-33, 36, 41, 45, 47, 48, 52, 53, and 55 having been previously canceled, and Claim 59 having been canceled herein. Claims 34, 39, 42, 50, 54, 56, 60 and 61 have been amended to more clearly define the invention.

Rejections of Claims 34, 35, 37-40, 42-44, 46, 49-51, 54, 56-58, and 60-61 35 U.S.C.§ 102

The Examiner has rejected Claims 34, 35, 37-40, 42-44, 46, 49-51, 54, 56-58, and 60-61 under 35 U.S.C. § 102 as being anticipated by Stern (U.S. Patent No. 5,981,956). The Examiner asserts that Stern discloses each element of applicants' claimed invention. Applicants have amended each independent claim, and as amended such claims distinguish over the cited art for the following reasons.

Stern specifically discloses that light collected from the object is dispersed by dichroic beam splitter 108 along different detection paths, such that the dispersed light is directed to detectors 124 and 140 (see FIGURE 1 from the Stern patent). Each of applicants' independent claims have been amended to recite that the light is dispersed such that a plurality of images are simultaneously formed *on different portions of a single detector*. Such an embodiment is clearly disclosed in applicants' specification as filed (for example, see FIGURES 3 and 13 in particular, as well as FIGURES 4-7, 9A-9B, 11, 14, 18 and 20, and the corresponding text in applicants' specification). Employing a single detector has advantages and requirements not taught or recognized by the prior art, thus the modifications to Stern's configuration to achieve an equivalent would not have been obvious to an artisan of ordinary skill.

For example, using a single detector in place of a plurality of detectors enables a more expensive, higher quality detector to be employed. As clearly described in applicants' specification, a time delay integration (TDI) detector represents a particularly preferred type of detector (for example, see applicants' FIGURE 21). Because such a detector acquires image data over time while an object moves relative to the imaging system, more image data can be acquired. Stern does not teach or suggest that any advantage can be obtained by replacing these detectors (126, 130, and 140) with a single detector, thus there is no support for concluding that such a modification would have been obvious.

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Furthermore, the use of a single detector requires a structural configuration that enables a plurality of images to be simultaneously acquired by a single detector. For example, the specification as filed discloses that in one embodiment:

> The angle of each dichroic beam splitter is set such that light reflected from it within the corresponding spectral bandwidth for the dichroic beam splitter is focused onto a different region of the detector. Since the present invention uses a narrow field angle in object space along axis 257, perpendicular to the axis of motion, many different spectral bandwidths can be simultaneously imaged onto a single detector. In this manner, each region on the detector may cover a different spectral bandwidth, while light is collected over the same field angle in object space (page36, first paragraph, discussing FIGURE14).

Clearly, the structural modifications required to enable a plurality of spectrally dispersed images to be simultaneously generated on different portions of a single detector are not trivial. Stern does not teach or suggest such a structure. While the pending claims are method claims, clearly to implement the step of simultaneously generating a plurality of images on different portions of a single detector, one must be able to produce or acquire a structure that can be used to implement such a step. As Stern does not teach or suggest such a structure, logically Stern cannot teach or suggest such a step.

The general element of simultaneously generating a plurality of images on different portions of a single detector is recited in each independent claim as amended (using variations in language; but the essential elements are present in each independent claim). The modifications to the cited art required to achieve a method including an equivalent step are not obvious in view of the teaching of the prior art. It is well accepted that dependent claims must be patentable for at least the same reasons as the claims from which they depend. Accordingly, the rejection of Claims 34, 35, 37-40, 42-44, 46, 49-51, 54, 56-58, and 60-61 under 35 U.S.C. § 102 as being anticipated by Stern should be withdrawn.

Furthermore, it should be noted that independent Claim 42 recites the step of:

collecting light from said object along a collection path, the light that is collected comprising light corresponding to each optical signaling component used to label the plurality of specific features that are part of the object, such light having been simultaneously collected

In other words, the object will include a plurality of specific features, each of which is uniquely labeled, and light from all of the features is simultaneously collected. In Stern's technique,

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an array of different features, each of which has been labeled, is sequentially scanned to acquire data corresponding to each feature. In general, the features are polymer sequences that are individually labeled. Significantly, while light from each dye used to label a specific polymer sequence is simultaneously collected, it appears that in Stern's technique each different polymer sequence is scanned individually. So if the array includes 100 different polymer sequences, then 100 sets of data are collected over a period of time. Thus, light from only a single polymer sequence is collected at any one time, even though a plurality of different polymer sequences are part of the array being scanned. The scanning functionality is disclosed in the final paragraph of column 6, as well as elsewhere in Stern's disclosure. Stern simply does not teach or suggest that light from a plurality of different features of an object is simultaneously collected, and that such light can be used to determine whether a specific feature is present on the object. In the context of the present invention, spectral signatures from a plurality of different features on a single object are simultaneously acquired, and the identity of each feature can be determined, even where two different features share a common signaling component.

For example, as indicated in applicants' FIGURE 2C, two different optical signaling components, A and B, can be used to uniquely label a plurality of different features, where the spectral signature 3A +B (or A-A-A-B) corresponds to a first feature, the spectral signature 2A + 2B (or A-A-B-B-) corresponds to a second feature, and the spectral signature A +3B (or A-B-B-B) corresponds to a third feature. Significantly, Claim 42 recites a method in which light from each of the three features is simultaneously collected, and the unique spectral signature associated with each different feature can be uniquely identified. Stern clearly discloses that a spectral signature including a plurality of components (i.e., a combination of different colored dyes) can be associated with a specific position in the array (i.e., a specific polymer sequence), but Stern does not teach or suggest that the spectral signatures of a plurality of different polymer sequences can be obtained simultaneously (i.e., without scanning).

Furthermore, it is not clear from Stern's disclosure whether Stern's apparatus can distinguish between the three different spectral signatures of FIGURE 2C. Stern's apparatus clearly can detect a spectral signature from a single polymer sequence where the spectral signature includes more than one optical signaling component (i.e., Stern's apparatus could detect a spectral signature comprising A+B). However, it is not clear that Stern's apparatus could differentiate the different intensities

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enabling the three different spectral signatures of FIGURE 2C to be distinguished. Even if Stern's apparatus could differentiate the different spectral signatures of FIGURE 2C, Stern does not teach or suggest that light (i.e. spectral signatures) from a plurality of different polymer sequences (i.e., features) corresponding to different locations on an object should be simultaneously collected (i.e., Stern appears to specifically disclose that the features of an object are scanned individually). Claim 42 distinguishes over the cited art for this additional reason.

Claims 39 and 50 have been amended to recite an additional aspect of the concepts disclosed in the pending application which further distinguish over Stern. Each claim recites that the step of analyzing comprises:

the step of determining if a multiplex of a spectral signature for each of the plurality of different optical signaling components is present in that image, such that the following spectral signatures can be differentiated, where A corresponds to a first optical signaling component, and B corresponds to a second optical signal component, where light defining all such spectral signatures has been simultaneously collected:

(a) a spectral signature comprising A-A-A-B;

(b) a spectral signature comprising A-A-B-B; and

(c) a spectral signature comprising A-B-B-B.

This relates to the discussion above with respect to Claim 42, however, the step of analyzing is emphasized over the step of collecting light from the object. The spectral signatures of subparagraphs (a)-(c) are identical to those illustrated in FIGURE 2C. With respect to the method and apparatus disclosed by Stern, if light from features labeled with the spectral signatures A-A-A-B, A-A-B-B, and A-B-B-B are acquired simultaneously, it is not clear whether Stern's apparatus is physically capable of differentiating the different spectral signatures. For example, assume A=red light, and B=blue light. Clearly, Stern's apparatus can detect a spectral signature A+B (red light is detected by a detector configured to respond only to red light, and blue light is detected by a detector configured to detect only blue light). However, Stern's apparatus is collecting light from only one feature/polymer sequence at a time, thus Stern's detectors need not be able to identify a spatial coordinate from which the red or blue light arose. Stern specifically discloses that photomultiplier tubes be used as detectors. Such devices simply identify a quantity of light received, not a spatial

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coordinate of the light received. Since the position of the stage/optics of Stern's device provides the spatial coordinate information, the detectors need not provide that information as well.

However, where two different features are labeled with a common signaling component (i.e., A-A-B-B and A-B-B-B), and light from features labeled with such spectral signatures is simultaneously acquired, the detector must provide both spatial and intensity information to enable the features labeled with such spectral signals to be distinguished.

With respect to Stern's analysis, because each feature is individually scanned, there is no need for the ability to spatially distinguish data from signaling components that are acquired simultaneously (i.e., according to Stern's method, signaling components from only one location are acquired at a time). Even if Stern's apparatus could be used to spatially distinguish signaling components from different features where the light from those features is simultaneously acquired, Stern does not teach or suggest such a step. With respect to determining the intensity of a particular signaling component, even if Stern's apparatus provides such information, Stern does not teach or suggest using *intensity* to distinguish different spectral signatures. Claims 49 and 50 distinguish over the cited art for these additional reasons.

<u>Analyzing Signatures Acquired Individually Vs. Analyzing Signatures Acquired Simultaneously</u>

It appears that the methods recited by applicants are distinguishable over the technique disclosed by Stern, because Stern acquires the spectral signature of different polymer sequences disposed at different locations on an array individually, whereas applicants' methods acquire the spectral signatures of different features disposed at different locations on an object simultaneously. Those techniques are distinctly different.

Applicants' technology enables a plurality of features on an object (such as a cell or planar array) to be labeled with different spectral signatures, where some of the spectral signatures include the same components (i.e., the same colors). Light from all of the features on the object is collected simultaneously, and that light is spectrally dispersed and used to generate a plurality of different images of the object. Those images can be used to determine what spectral signatures are present on the object, enabling the specific features on the object to be identified. Stern's technique can identify spectral signatures of all of the features on an object, however, Stern's technique requires that the light from individual features must be collected individually (the scanning step). Significantly, applicants' technique does not require the scanning step disclosed by Stern, thus the time required to

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acquire data (i.e., light) from the plurality of features on an object is significantly reduced (thus, applicants' technique enables objects to be analyzed more rapidly).

Consider, for example, a Cell #1, which has been labeled at four different locations. Note each location can be considered to be a different feature. FIGURE 3 of the pending application shows six different images of two different cells (violet, indigo, blue, green, yellow, and red images) that have been simultaneously acquired for each cell (by spectrally dispersing light from each cell before imaging and detecting). Each cell includes four different features labeled by different combinations of blue, green, yellow and red optical signaling components. Referring again to Cell #1 (cell 300 of FIGURE 3), Location 1 (feature 310) is labeled with blue (C1L1=B), Location 2 (feature 308) is labeled with green (C1L2=G), Location 3 (feature 304) is labeled with yellow (C1L3=Y), and Location 4 (feature 306) is labeled with red (C1L4=R). Cell 1 is thus labeled with blue, green, yellow and red, and the ratios of the different colors (blue:green:yellow:red) are: 1:1:1:1.

Significantly, applicants' technique collects light from each feature simultaneously. Stern's technique would require each locations/feature to be scanned individually (that is, light from each different feature would need to be acquired individually). The techniques are related, but not identical.

Furthermore, if Stern's technique were modified to acquire light from more than one polymer sequence simultaneously, it is not clear that Stern's apparatus would be able to spatially identify different optical signaling components. For example, assume polymer sequence 1 is labeled with blue, green, yellow, and red (PS1=BGYR), and polymer sequence 2 is labeled with blue and red (PS2=BR). Stern's apparatus clearly can be configured to detect blue, green, yellow and red light using four different detectors and filters, such that one detector responds only to blue light, another detector responds only to green light, still another detector responds only to yellow light, and the final detector responds only to red light. However, because Stern relies on the position of the stage to determine the location of the specific polymer sequence, it is not apparent whether Stern's apparatus can distinguish the red light from polymer sequence 1 from the red light of polymer sequence 2, if light from polymer sequence1 and light from polymer sequence 2 are acquired simultaneously. Note that Stern specifically indicates that the detectors be photomultiplier tubes. Such elements will simply respond to the presence of light, as opposed to providing a spatial coordinate. In other words, it appears that Stern's detectors would simply respond to red light, and not be able to identify from

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which location the light arose, if light from a plurality of different locations is simultaneously acquired.

Accordingly, all of the claims now remaining in the application define patentable subject matter that is neither anticipated nor obvious in view of the prior art cited. The Examiner is thus requested to pass the present application to issue in view of the amendments and the remarks submitted above. If there are any questions that might be addressed by a further telephone interview, the Examiner is invited to telephone the undersigned attorney, at the number listed below.

Respectfully submitted,

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